

**EPA/600/R-99/086**  
**May 2000**

**ASSESSMENT OF HEALTH EFFECTS OF PESTICIDE EXPOSURE  
IN YOUNG CHILDREN**

Proceedings of a Workshop held in El Paso, Texas in December 1997

Edited by

David Otto, Rebecca Calderon, Pauline Mendola and Elizabeth Hilborn

Epidemiology and Biomarkers Branch  
Human Studies Division  
National Health and Environmental Effects Research Laboratory  
U.S. Environmental Protection Agency  
Research Triangle Park, NC 27711

National Health and Environmental Effects Research Laboratory  
Office of Research and Development  
U.S. Environmental Protection Agency  
Research Triangle Park, NC 27711

This document is the Executive Summary for the *Assessment of Health Effects of Pesticide Exposure in Young Children*, Proceedings of a Workshop held in El Paso, Texas in December 1997.

Copies of the complete text may be obtained by contacting:

Walter Breyer  
U.S. Environmental Protection Agency  
NHEERL/HSD/MD-58C  
Research Triangle Park, NC 27711

Tel: 919/966-8575  
FAX: 919/966-0655  
E-mail: [breyer.walter@epa.gov](mailto:breyer.walter@epa.gov)

## **EXECUTIVE SUMMARY**

### **WORKSHOP ON THE ASSESSMENT OF HEALTH EFFECTS OF PESTICIDE EXPOSURE IN YOUNG CHILDREN**

#### **Background**

Pesticides are a broad group of chemicals used to kill insects, fungus and undesirable plant species; they are by design, biologically active compounds. Millions of pounds are applied in agricultural, industrial, institutional, commercial, and residential settings within the United States (US) each year. Pesticide exposure is ubiquitous via contamination of food, soil, air, and water, yet the health effects of chronic, low-dose exposure are unknown. There is growing concern that current tolerance levels may not be sufficient to protect the health of children.

Children are at greater risk than adults for increased exposure to pesticides. Hand-to-mouth activity increases the risk of pesticide exposure by the oral route. Children have a proportionally greater surface area and tend to have more dermal contact with soil and indoor floor surfaces than adults. Children consume more food and beverage as a portion of their body weight than adults. Foods such as fruits and fruit juices may form a large part of a young child's diet and represent a major source of pesticide exposure. Children may be particularly vulnerable to the effects of pesticides due to rapidly maturing organ and nervous systems. Children's metabolism of pesticides is not well understood. Differences in biotransformation and elimination may result in children experiencing a greater toxic effect than adults.

Children along the US-Mexican border may be at increased risk for pesticide exposure due to the prevalence of year-round agriculture in this region. Research efforts to determine if there are measurable health effects associated with chronic low dose exposure to pesticides will initially be focused in the border region as part of the Border XXI Program.

During December 7-9 1997, the Environmental Health Workgroup sponsored a workshop on the assessment of health effects of pesticide exposure in young children to discuss the current state of the science, and to identify priorities for future research.

#### **Workshop Structure and Goals**

Experts from a variety of fields participated in the workshop. The three-day meeting was structured to include discussion of pesticide exposure measurement, potential health effects in the pediatric population, and current research efforts in the US-Mexican border area. Small workgroups were organized to address five health endpoint domains: cancer, neurological, respiratory, immunologic, and developmental effects. After day one, the respiratory and immunology groups combined to discuss areas of subject overlap. Workgroup members were selected to represent multiple areas of expertise: epidemiology, exposure assessment, clinical medicine, and those with experience conducting research along the US-Mexican Border.

#### **Day One**

The first day focused on issues related to the study of children. Dr. Bornschein gave the keynote address: 'Issues in Pediatric Epidemiology' based on his work with lead-exposed children. Dr. David Bellinger discussed potential methods for the neurobehavioral assessment of children at different stages of development. Dr. Anthony Horner's presentation focused on published studies of immunotoxic effects of pesticides in human and animal models. Dr. Antolin Llorente reviewed the neurotoxicant effects of pesticides in adults and the need for well-designed studies of children exposed during periods of rapid neurologic development. Dr. Maria Martinez discussed techniques available to measure pulmonary

function in children of various ages. Dr. Jonathan Buckley presented information about the study of children diagnosed with cancer and highlighted the difficulties associated with the evaluation of pesticide exposure assessment in these children.

### **Workgroup Reports      Day One - Health Effects**

The focus of the workgroups on Day One was to identify lists of health endpoints that were relevant and measurable in young children and infants. There is very little documentation of health effects related to low-dose pesticide exposure in young children, so workgroup members extrapolated from their knowledge of occupational exposure studies, acute toxicity reports, and animal studies.

**Cancer:** In the United States, cancer is the second leading cause of death for children between the ages of one and 14 years. Although overall cancer rates have generally been declining, the rate of childhood cancer has increased in North America. Specific cancer diagnoses such as: acute lymphoid leukemia, tumors of the central nervous system and bone would be of particular interest in the study of environmental exposures.

**Developmental:** Exposures that may occur during the prenatal period or infancy may have the greatest impact on the developing child. The following developmental health endpoints are listed in priority order as defined by the workgroup: birth defects, stillbirths, and spontaneous abortion; mental, motor, adaptive development; growth; language; birth weight related to gestational age; social development; infant mortality; puberty, age at menarche and development of secondary sex characteristics.

**Neurology:** The workgroup identified assessment tools appropriate for evaluation of children in various age groups. The Bayley Scales of Infant Development, Wechsler Preschool and Primary Scales of Intelligence-Revised, the Wide Range Assessment of Visual Motor Abilities, Wide Range Assessment of Memory and Learning, Peabody Developmental Motor Scales, Visual acuity, Wechsler Intelligence Scales for Children, 3rd ed., visual contrast sensitivity, and Neurobehavioral Evaluation System all received priority rankings.

**Immunology:** The workgroup identified immunologically-associated health endpoints of interest. These included: asthma (reactive airway disease); allergy; primary immunodeficiency; contact dermatitis; lupus erythematosus; inflammatory bowel disease; infectious diseases; and adverse reproductive outcomes.

**Respiratory:** The respiratory workgroup discussed both the utility of validated disease endpoints and self-reported symptomatology in assessing overall pulmonary health. The workgroup discussed four respiratory diseases: upper respiratory infection, acute bronchitis, asthma, and interstitial lung disease.

### **Day Two - Research issues**

The keynote address, 'Health Effects of Pesticides' was delivered by Dr. Donald Ecobichon. He discussed the health effects of acute pesticide poisonings in adult agricultural workers. He emphasized that the research challenge will be to develop methods to measure subtle psychologic, behavioral, and neurologic deficits in children exposed to lower doses of toxic mixtures of the 'inert' and active ingredients in pesticide formulations. Dr. Stephanie Padilla reported that her laboratory is investigating the effects of sub-lethal doses of chlorpyrifos on young rats. Young, postnatal rats are more sensitive to organophosphate pesticides than adults. Differences in levels of detoxification enzymes may account for some of this observed effect.

Dr. Jim Quackenboss discussed the design of a Children's Pesticide Exposure Survey. He discussed that one of the major difficulties of research in the field of health effects of pesticides on children has been

the difficulty in selecting 'high' exposure individuals from the general population. Mr. Gary Robertson reported the results of a survey of pesticide use near the US-Mexico border. Methods used to evaluate pesticide usage were different in each state; some states collect actual usage data, in others, usage was estimated from agricultural crop records and acreage under cultivation. Dr. Mary Kay O'Rourke discussed her current exposure assessment projects. These include: the National Human Exposure Assessment Survey, a survey of residents along the US-Mexican border in Arizona, a Children's Pesticide Survey in Yuma, Arizona, and multiple projects requested by communities along the border, studying health effects such as asthma, diabetes mellitus and lupus erythematosus. Dr. Jim VanDerslice raised issues related to studying populations along the U.S.-Mexican Border. He stressed that although the Border Region is referred to as a single entity, it is actually a very diverse collection of communities along a 2000 mile long corridor. Dr. Rob McConnell discussed cultural considerations in the conduct of epidemiologic studies along the U.S.-Mexican Border. Dr. James Ellis highlighted potential resources for pediatric research in the Border area. He emphasized the need to build trust between researchers and community members before research is initiated.

### **Workgroup Reports Day Two- Development of Strawman Study Proposals**

The second day of the workshop was designed to integrate selected health endpoints identified during the Day One workgroup sessions into a collection of potential study designs for implementation along the border region.

Cancer: The workgroup outlined and discussed several possible types of studies including:

- 1) Use of existing cancer data bases.
- 2) An ecological study could compare pesticide usage in border and non-border regions and determine if there is a difference in cancer patterns in these areas.
- 3) A case-control study: cancer cases could be obtained from clinics and hospitals.
- 4) A prospective cohort study: exposure would be measured with the use of a biomarker and incident cases of cancer recorded.
- 5) A case control design could identify children with leukemia and determine if they have a higher level of V(D)J recombinase mediated chromosomal rearrangements.

Developmental: Proposed studies were classified as analytic, descriptive or capacity building.

#### **Analytic Studies**

- 1) A prospective prenatal cohort. The study hypothesis would be: pesticide exposure is related to delayed and/or altered development and long term developmental problems.
- 2) A poisoned children case study. The study hypothesis would be: there are persistent neurobehavioral and neurodevelopmental sequelae of acute pesticide exposure.
- 3) A prospective nested case-control study of symptomatic children. The study hypothesis would be: there are no developmental differences between symptomatic children with detectable urinary metabolites of organophosphate pesticides and symptomatic children without detectable urinary metabolites.

#### **Descriptive Studies**

- 1) A cross-sectional study of any correlation between levels of pesticides, anticholinesterase, and related enzymes in maternal and infant biologic samples.
- 2) A descriptive cross-sectional study using a Geographic Information System approach of infant health status. The main hypothesis is that infant mortality and birth weight are not different in areas with high agricultural pesticide use compared to geographic areas with lower agricultural pesticide use.

#### **Capacity Building**

- 1) Pesticide Dose: a summary of pesticide dose information in young children is needed.
- 2) Adaptation of neurodevelopmental tests to populations within the border region.

Neurology: The Neurology workgroup discussed three study designs--(1) a retrospective cohort design, (2) a cross-sectional study, and (3) a longitudinal cohort study. The basic hypothesis addressed by these studies is that exposure to pesticides produces neurotoxic effects in children.

- 1) Retrospective Acute, High-exposure Cohort Study. A retrospective cohort study of a group of children with clearly defined, high-level exposure will be selected for an initial study to determine whether or not pesticide exposure produces neurotoxic effects in young children.
- 2) Cross-sectional Chronic, Low-exposure Study. An exposure questionnaire will be administered to parents of children aged 1.5-2.5 years to select three groups--high, middle and low exposure deciles (10%). The Bayley Test is recommended for neurobehavioral assessment of children. Exposure measures should include house dust and urine samples for biological measures.
- 3) Longitudinal Cohort Study. 100 children living in a high-risk area could be selected. The Bayley Test would be administered at 3-month intervals for one-two years. Urine samples should be obtained at each testing for measurement of OP levels, metabolites and a-esterases.

Immunology / Respiratory: The group agreed on some study designs to evaluate the association between pesticide exposure and immunological and pulmonary health effects.

- 1) Cross sectional study, questionnaire derived exposure combined with self-reported health endpoints. Exposure assessment supplemented by GIS and some environmental sampling. Hypothesis: the prevalence of asthma and other diseases will be higher in individuals with increased pesticide exposure.
- 2) A case-control study based on exposure status. The study hypothesis: pesticide exposure increases the incidence of and/ or exacerbates pre-existing asthma.
- 3) A methacholine challenge test to objectively assess airway reactivity would be administered to a group of healthy children. A case - control study would follow with case status assigned to those with airway hyper reactivity. The study hypothesis is that pesticide exposure contributes to airway hyper reactivity.
- 4) Cross sectional study of children < 1 years of age as a pilot for a longitudinal study of a birth cohort. The study hypothesis: pesticide exposure affects the development of the immune system in infants resulting in altered antibody response to vaccine administration and increased incidence of infectious disease.

### **Day 3- Group discussion**

The following seven research priorities were assembled based on reports from workgroups and individual participants' comments during the day's discussion.

- 1) The development of efficient methods for screening children for exposure status
- 2) Questionnaire development and validation in Border communities
- 3) Targeted environmental sampling to increase efficiency
- 4) Validation of biochemical measures of exposure
- 5) The need to establish normal ranges for health endpoints
- 6) The development of sophisticated modeling techniques to more accurately predict the health effects of exposure to multiple pesticides by multiple exposure routes
- 7) Studies must have adequate power to detect subtle pesticide-associated health effects

Workshop members stressed that public health officials and health care providers from the border community are requesting better exposure measurements. They would like to know the extent of environmental pesticide contamination, would like to know the potential health effects associated with pesticide exposure, and if current levels of pesticide exposure are causing health problems.